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U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM 42014 mEB

Examiner # (Mandatory): 65525 Requester's Full Name: E Bernhardt

Art Unit 1624 Location (Bldg/Room#): 4E15 Phone (circle 305 306 (308) 4 714

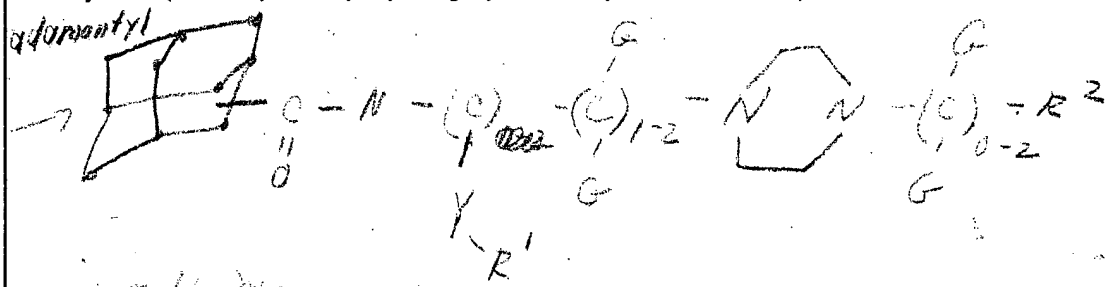
Serial Number: 09/706683 Results Format Preferred (circle): PAPER DISK E-MAIL

Title of Invention _____

Inventors (please provide full names): _____

Earliest Priority Date: _____

Keywords (include any known synonyms registry numbers, explanation of initialisms):



Search Topic:

Please write detailed statement of the search topic, and the concept of the invention. Describe as specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc., if known. You may include a copy of the abstract and the broadcast or most relevant claim(s).

R2 = phenyl or naphthyl - optionally substd.

RECEIVED
MAY - 9 2001
(STIC)

STAFF USE ONLY

Searcher: JOHN DANZMAN

Searcher Phone #: _____

Searcher Location: _____

Date Picked Up: 5-11-01

Date Completed: 5-11-01

Clerical Prep Time: 25

Terminal Time: _____

Number of Databases: 25

Type of Search

_____ N.A. Sequence
_____ A.A. Sequence
1 Structure (#)
_____ Bibliographic
_____ Litigation1
_____ Fulltext
_____ Procurement
_____ Other

Vendors (include cost where applicable)

✓ STN
_____ Questel/Orbit
_____ Lexis/Nexis
_____ WWW/Internet
_____ In-house sequence systems (list)
_____ Dialog
_____ Dr. Link
_____ Westlaw
_____ Other (specify)

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                  SAV L5 BERN706/A TEMP
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CAOLD

zero hits

Berlstein

zero hits

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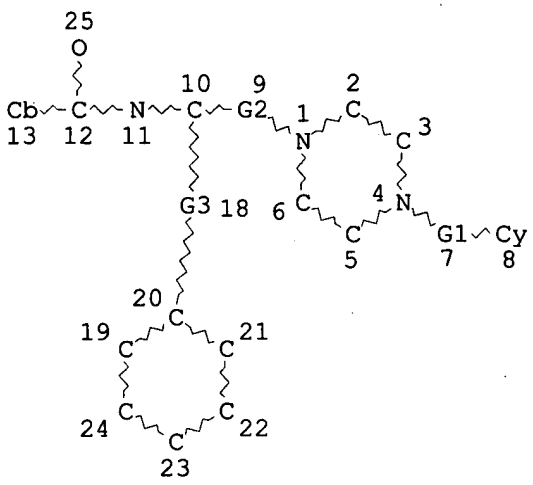


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REP G3=(0-4) A
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STEREO ATTRIBUTES: NONE
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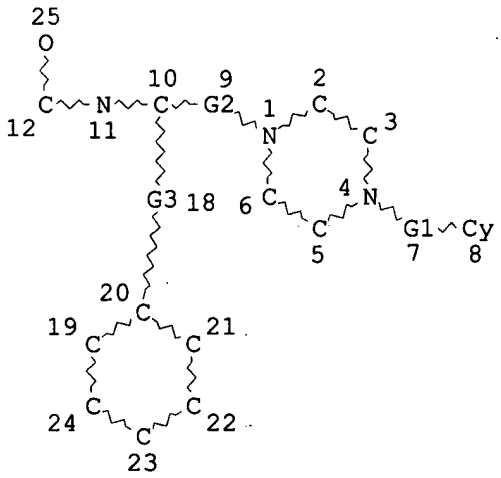


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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS  20

STEREO ATTRIBUTES: NONE
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L6            5 SEA FILE=REGISTRY SUB=L5 SSS FUL L1


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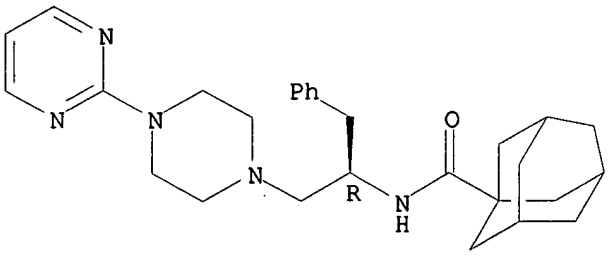
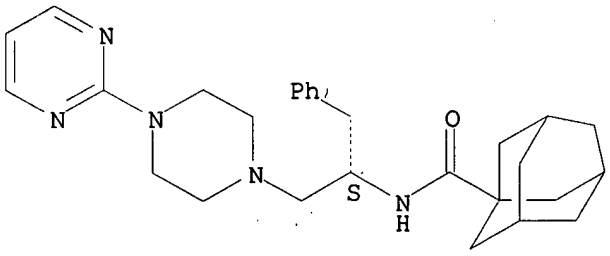
L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
AN 1999:757952 CAPLUS
DN 132:117085
TI Synthesis and SAR of Adatanserin: Novel Adamantyl Aryl- and Heteroarylpiperazines with Dual Serotonin 5-HT1A and 5-HT2 Activity as Potential Anxiolytic and Antidepressant Agents
AU Abou-Gharbia, Magid A.; Childers, Wayne E., Jr.; Fletcher, Horace; McGaughey, Georgia; Patel, Usha; Webb, Michael B.; Yardley, John; Andree, Terrance; Boast, Carl; Kucharik, Robert J.; Marquis, Karen; Morris, Herman; Scerni, Rosemary; Moyer, John A.
CS Chemical Sciences and CNS Disorders, Wyeth-Ayerst Research, Princeton, NJ, 08543-8000, USA
SO J. Med. Chem. (1999), 42(25), 5077-5094
CODEN: JMCMAR; ISSN: 0022-2623
11/28/99
PB American Chemical Society
DT Journal
LA English
OS CASREACT 132:117085
AB Several novel functionalized adamantyl aryl- and heteroarylpiperazine derivs. were prepd. and examd. in various receptor binding and behavioral tests to det. their serotonin receptor activities. Many compds. demonstrated modest to high affinity for 5-HT1A receptors. 2-[4-(2-Pyrimidinyl)-1-piperazinyl]ethyl adamantyl-1-carboxylate demonstrated relatively high affinity for 5-HT1A receptors (Ki = 8 nM) and acceptable selectivity vs. D2 receptors (Ki = 708 mM); however, it lacked in vivo activity in serotonergic behavioral models. In contrast, WY-50,324 (SEB-324, adatanserin) (adamantyl-1-carboxylic acid 2-[4-(2-pyrimidinyl)-1-piperazinyl]ethylamide) (I) and adamantyl-1-carboxylic acid 2-[4-(2-methoxyphenyl)-1-piperazinyl]ethylamide demonstrated high affinity for 5-HT1A binding sites (Ki = 1 nM for both) and moderate affinity for 5-HT2 receptors (Ki = 73 and 75 nM, resp.). Both compds. also demonstrated partial 5-HT1A agonist activity in vivo in rat serotonin syndrome and 5-HT2 antagonist activity in quipazine- and DOI-induced head shake paradigms. The selective 5-HT1A partial agonist and 5-HT2 antagonist activity of I was accompanied by significant anxiolytic activity in an animal conflict model. On the basis of this profile, compd. 9 entered development as a combined anxiolytic and antidepressant agent.
IT **256351-85-6P 256351-86-7P 256351-87-8P 256351-88-9P 256351-89-0P**
RL: BPR (Biological process); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(synthesis and SAR of adatanserin by prepn. of novel adamantyl and aryl- and heteroarylpiperazines with dual serotonin 5-HT1A and 5-HT2 activity as potential anxiolytic and antidepressant agents)
RN 256351-85-6 CAPLUS
CN Tricyclo[3.3.1.13,7]decane-1-carboxamide, N-[(1R)-1-(phenylmethyl)-2-[4-(2-pyrimidinyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



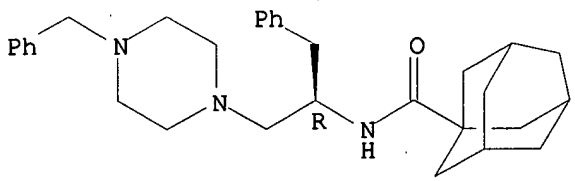
RN 256351-86-7 CAPLUS
CN Tricyclo[3.3.1.13,7]decane-1-carboxamide, N-[(1S)-1-(phenylmethyl)-2-[4-(2-pyrimidinyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 256351-87-8 CAPLUS
CN Tricyclo[3.3.1.13,7]decane-1-carboxamide, N-[(1R)-1-(phenylmethyl)-2-[4-(phenylmethyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



●2 HCl

RN 256351-88-9 CAPLUS
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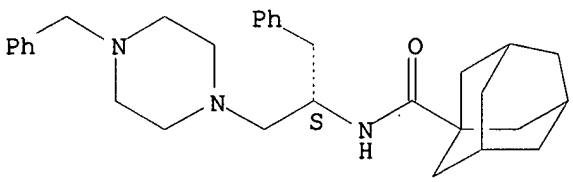
Absolute stereochemistry. Rotation (+).



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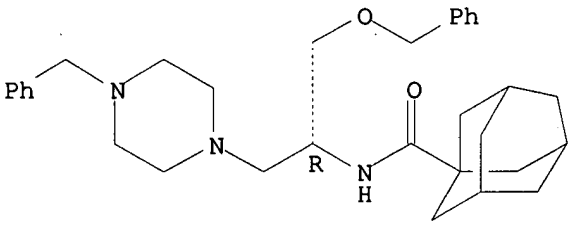
RN 256351-89-0 CAPLUS
CN Tricyclo[3.3.1.13,7]decane-1-carboxamide, N-[(1R)-1-[(phenylmethoxy)methyl]-2-[4-(phenylmethyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



●2 HCl

RE.CNT 85
RE
(1) Abou-Gharbia, M; US 4797489 1989 CAPLUS
(4) Albinsson, A; Eur J Pharmacol 1994, V261, P285 CAPLUS
(6) Barrett, J; Drug Dev Res 1991, V24, P179 CAPLUS
(7) Barrett, J; Psychopharmacology 1993, V112, P1 CAPLUS
(8) Bojarski, A; Wiad Chem 1994, V48, P419 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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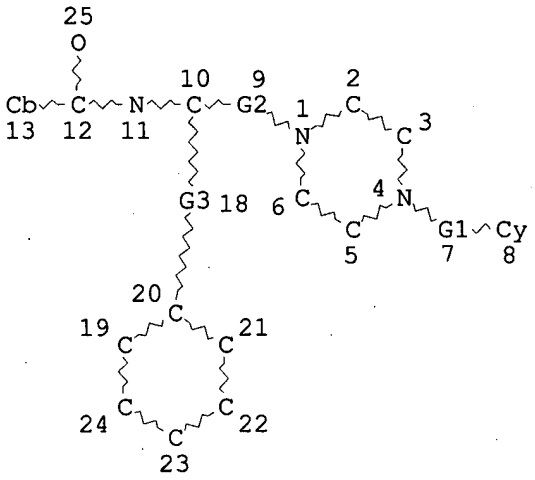


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DEFAULT MLEVEL IS ATOM
GGCAT   IS PCY  SAT  AT  13
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  21

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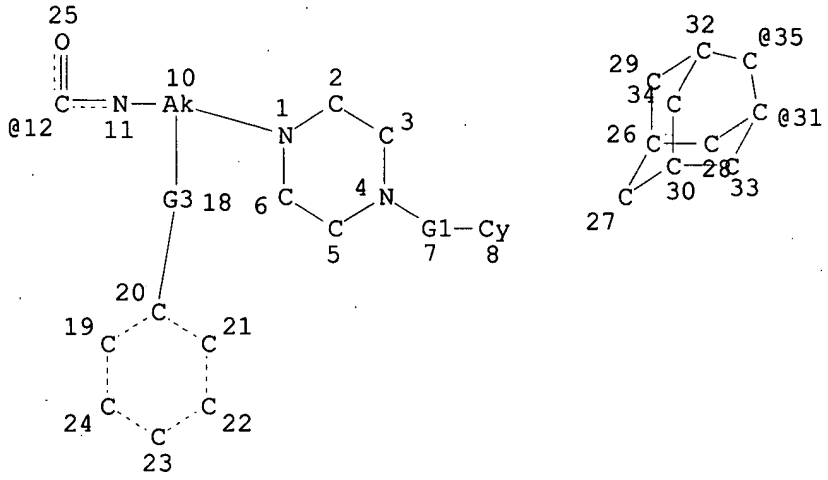

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NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
MLEVEL IS ATOM ON RING NODES AND RING GROUPS
MLEVEL IS CLASS ON CHAIN NODES AND CHAIN GROUPS
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L7 13 SEA FILE=MARPAT SSS FUL L4 (MODIFIED ATTRIBUTES)
L8 2 SEA FILE=MARPAT ABB=ON PLU=ON L7/COMP

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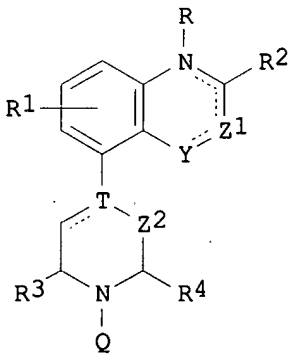
L8 ANSWER 1 OF 2 MARPAT COPYRIGHT 2001 ACS
ACCESSION NUMBER: 130:223299 MARPAT
TITLE: Preparation of 5-piperazinotetrahydroquinolines and analogs as 5-HT1 receptor agonists
INVENTOR(S): Feenstra, R. W.; Visser, G. M.; Kruse, C. G.; Tulp, M.
T. M.; Long, S. K.
PATENT ASSIGNEE(S): Duphar International Research B.V, Neth.
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 900792	A1	19990310	EP 1998-202832	19980824
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2246126	AA	19990302	CA 1998-2246126	19980828
JP 11147871	A2	19990602	JP 1998-259105	19980831
US 6214829	B1	20010410	US 1998-144076	19980831

PRIORITY APPLN. INFO.: EP 1997-202704 19970902
GI

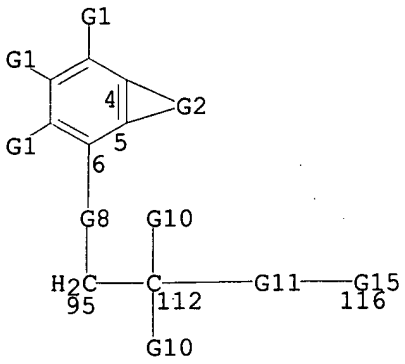


I

AB Title compds. [I; Q = CH2CR5R6ZR7; R,R3,R4 = H or alkyl; R1 = H or F; R2 = H, alkyl, oxo (sic); RR2 = bond; R5,R6 = H, alkyl, alkylphenyl; R7 = cyclic group (sic), (hetero)aryl, adamantyl, etc.; T = N or C (sic); Y = C, O, N, or S (sic); Z = CH2O, CH2CO, NHCO, etc.; Z1 = (CR'')p; R'' = H or alkyl; Z2 = (CH2)n; n = 1 or 2; p = 0-2; dashed lines = optional bond(s)] were prepd. Thus, 5-(1-piperazinyl)-1,2,3,4-tetrahydroquinoline was alkylated by Cl(CH2)3COC6H4F-4 to give I [Q = (CH2)3COC6H4F-4; R-R4 = H, T = N, Y = Z1 = Z2 = CH2, dashed lines = null]. Data for biol. activity of

I were given.

MSTR 1



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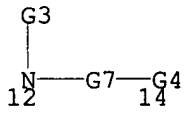
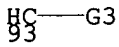


G4 = CH2
G5 = N
G7 = 93



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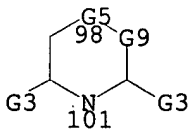
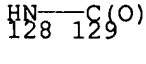


G9 = (1-2) CH2
G10 = alkyl<(1-3)> (SR Ph)
G11 = 128-112 129-116



G15 = adamantyl (SO (1-) G16)
DER: and salts
MPL: claim 1

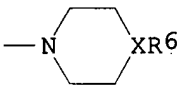
NTE: substitution is restricted

REFERENCE COUNT: 13
REFERENCE(S): (1) American Home Food Products Inc; EP 0785195 A 1997
CAPLUS
(2) American Home Products; US 5486518 A 1996 CAPLUS
(3) American Home Rpoducts; US 5519025 A 1996 CAPLUS
(4) Duphar Int Res; WO 9736893 A 1997 CAPLUS
(5) Duphar International Research; EP 0372657 A 1990 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 2 MARPAT COPYRIGHT 2001 ACS
ACCESSION NUMBER: 120:299317 MARPAT
TITLE: Preparation of amino acid amide derivatives as tachykinin antagonists
INVENTOR(S): Mase, Toshasu; Kubota, Koichi; Imanishi, Naoki; Tomioka, Kenichi
PATENT ASSIGNEE(S): Yamanouchi Pharma Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 32 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

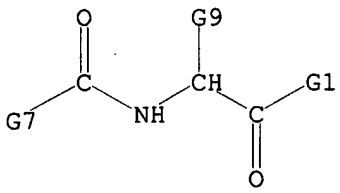
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05294915	A2	19931109	JP 1992-129510	19920421

GI

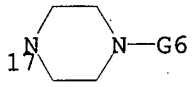
Q= 

AB Amino acid amide derivs. R3NHCHR4CONR1R2 [R1 = H, lower alkyl, cycloalkyl, aralkyl; R2 = lower alkyl, AR5, NR1R2, Q; A = single bond, linear or branched alkyl alkylene; R5 = (un)substituted Ph or benzhydryl, cycloalkyl; X = N, CH; R6 = H, lower alkyl, Ph, aralkyl; R3 = H, CO2R7, CONHR7, COR8; R7 = lower alkyl, optionally crosslinked cycloalkyl(alkyl), Ph, aralkyl; R8 = R7, (un)substituted fused heterocyclyl; R4 = (un)substituted CH2Ph, benzhydryl, Ph, C3-10 alkyl, cycloalkyl, (un)substituted fused heterocyclylmethyl], optical isomers, or salts thereof, antagonizing tachykinin receptors, particularly substance P, neurokinin A, or neurokinin B receptor, and useful for treating tachykinin-mediated diseases, are prepd. Thus, iso-Bu chloroformate was added to a mixt. of Boc-Phe-OH, N-methylmorpholine, and THF under ice-MeOH cooling; the mixt. was stirred at at -15.degree. to -20.degree. and reacted with N-methylbenzhydrylamine at room temp. for 2 h to give phenylalaninamide deriv. Boc-Phe-NMeCHPh2 (I). I showed IC50 of 0.58 .mu.M for inhibiting substance P-induced contraction of guinea pig's ileum. A total of 43 I were prepd. Tablet and capsule formulations contg. I were given.

MSTR 1



G1 = 17



G6 = Ph
G7 = 1-adamantyl
G9 = CH2Ph (SO)
DER: or salts
MPL: claim 1
STE: or optical isomers